

What is claimed is:

1. A soluble fusion protein comprising a bacteriophage coat protein covalently linked to a single-chain T cell receptor, wherein the single-chain T cell receptor comprises a V- α chain covalently linked to a V- β chain by a peptide linker sequence.

2. The soluble fusion protein of claim 1, wherein the C-terminus of the V- α chain is covalently linked by the peptide linker sequence to the N-terminus of V- β chain.

3. The soluble fusion protein of claim 1, wherein the C-terminus of the V- β chain is covalently linked by the peptide linker sequence to the N-terminus of the V- α chain.

4. The soluble fusion protein of claim 2 further comprising a C- β chain fragment covalently linked between the C-terminus of the V- β chain and the N-terminus of the bacteriophage coat protein.

5. The soluble fusion protein of claim 2 further comprising a C- α chain fragment covalently linked between the C-terminus of the V- α chain and the N-terminus of the peptide linker sequence.

6. The soluble fusion protein of claim 2, wherein the fusion protein further comprises at least one protein tag.

7. The soluble fusion protein of claim 2, wherein the peptide linker sequence contains from approximately 2 to 20 amino acids.

8. The soluble fusion protein of claim 1, wherein the bacteriophage coat protein is gene III or gene VIII protein.

9. A soluble fusion protein comprising covalently linked in sequence: 1) a V- α chain, 2) a peptide linker sequence, 3) a V- β chain and 3) a bacteriophage gene III protein.

10. The soluble fusion protein of claim 9 further comprising a C- β chain fragment covalently linked between the C-terminus of the V- β chain and the N-terminus of the bacteriophage gene III protein.

11. The soluble fusion protein of claim 10, further comprising a protein tag covalently linked to the C-terminus of the C- β fragment and the N-terminus of the bacteriophage gene III protein.

12. The soluble fusion protein of claim 9 further comprising a first protein tag covalently linked between the C-terminus of the V- β chain and the N-terminus of the bacteriophage gene III protein, and a second protein tag covalently linked to the C-terminus of the fusion protein.

13. A soluble fusion protein comprising covalently linked in sequence: 1) a V- α chain, 2) a peptide linker sequence, 3) a V- β chain, and 4) a bacteriophage gene VIII protein.

14. A soluble fusion protein comprising covalently linked in sequence: 1) a V- α chain, 2) a peptide linker sequence, 3) a V- β chain covalently linked to a C- β chain fragment, and 4) a bacteriophage gene VIII protein.

15. A soluble fusion protein comprising covalently linked in sequence: 1) a V- α chain covalently linked to a C- α chain fragment, 2) a peptide linker sequence, 3) a V- β chain covalently linked to a C- β chain fragment, and 4) a bacteriophage gene VIII protein.

16. The soluble fusion protein of claim 13 further comprising a first protein tag covalently linked to the C-terminus of the V- β chain and the N-terminus of the gene VIII protein, and a second protein tag covalently linked to the C-terminus of the fusion protein.

17. The soluble fusion protein of claim 14 or 15 further comprising a protein tag covalently linked to the C-terminus of the C- β chain fragment and the N-terminus of the gene VIII protein.

18. The soluble fusion protein of claim 2, wherein the V- α and V- β chains are isolated from cytotoxic T cells.

19. A single-chain T cell receptor produced by cleaving the one or more protein tags from the soluble fusion protein of claim 6.

20. The single-chain T cell receptor of claim 19, wherein the single-chain T cell receptor has been humanized.

21. A DNA segment comprising a sequence encoding a soluble fusion protein, the soluble fusion protein comprising a bacteriophage coat protein covalently linked to a single-chain T cell receptor, wherein the DNA segment further comprises an operably linked promoter and linker sequence.

22. A DNA segment comprising a sequence encoding a soluble fusion protein comprising covalently linked in sequence: 1) a V- α chain, 2) a peptide linker sequence, 3) a V- β chain and 3) a bacteriophage gene III protein.

23. A DNA segment comprising a sequence encoding a soluble fusion protein comprising covalently linked in sequence: 1) a V- α chain, 2) a peptide linker sequence, 3) a V- β chain, and 4) a bacteriophage gene VIII protein.

24. A DNA segment comprising a sequence encoding a soluble fusion protein comprising covalently linked in sequence: 1) a V- α chain, 2) a peptide linker sequence, 3) a V- β chain covalently linked to a C- β chain fragment, and 4) a bacteriophage gene VIII protein.

25. A DNA segment comprising a sequence encoding a soluble fusion protein comprising covalently linked in sequence: 1) a V- α chain covalently linked to a C- α chain fragment, 2) a peptide linker sequence, 3) a V- β chain covalently linked to a C- β chain fragment, and 4) a bacteriophage gene VIII protein.

26. The DNA segment of claim 23 further comprising a sequence encoding a protein tag covalently linked between the 3' end of the sequence encoding the V- β chain and the 5' end of the sequence encoding the bacteriophage gene VIII protein.

27. The DNA segment of claim 24 or 25 further comprising a sequence encoding a protein tag covalently linked between the 3' end of the sequence encoding the C- β chain fragment and the 5' end of the sequence encoding the bacteriophage gene VIII protein.

28. The DNA segment of claim 26 further comprising sequence encoding a protein tag covalently linked to the 3' end of the sequence encoding the fusion protein.

29. A DNA vector comprising the DNA segment of claim 21.

30. The DNA segment of claim 21, wherein the promoter and linker are *phoA* and *pelB* from *E. coli*, respectively.

31. A bacteriophage library comprising bacteriophages displaying soluble fusion proteins, wherein each of the soluble fusion proteins comprises a bacteriophage coat protein covalently linked to a single-chain T cell receptor, wherein each single-chain T cell receptor comprises a V- α chain covalently linked to a V- β chain by a peptide linker sequence.

32. The bacteriophage library of claim 31, wherein the C-terminus of the V- α chain is covalently linked by the peptide linker sequence to the N-terminus of V- β chain.

33. The bacteriophage library of claim 31, wherein the C-terminus of the V- β chain is covalently linked by the peptide linker sequence to the N-terminus of the V- α chain.

34. The bacteriophage library of claim 31, wherein the soluble fusion protein further comprises at least one protein tag.

35. The bacteriophage library of claim 31, wherein the V- α and V- β chains are isolated from an immunologically naive mammal.

36. The bacteriophage library of claim 31, wherein the V- α and V- β chains are isolated from a mouse.

37. The bacteriophage library of claim 31, wherein the mouse includes a transgene capable of expressing an HLA-A2 antigen complex.

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38. The bacteriophage library of claim 31, wherein the V- α and V- β chains are obtained from a human suffering from or suspected of having cancer, an infectious disease, an autoimmune disorder, or an allergy.

39. The bacteriophage library of claim 31, wherein the infectious disease is an infection by an RNA or DNA virus.

40. The bacteriophage library of claim 39, wherein the RNA virus is a human immunodeficiency virus.

41. The bacteriophage library of claim 39, wherein the DNA virus is selected from the group consisting of cytomegalovirus, adenovirus, polyoma virus, influenza, or pox virus.

42. The bacteriophage library of claim 31, wherein the bacteriophage coat protein is gene VIII protein.

43. A kit comprising the bacteriophage display library of claim 31, a host cell sample, and directions for using the kit.

44. A bacteriophage library comprising bacteriophages displaying soluble fusion protein muteins, wherein each of the soluble fusion protein muteins comprises a bacteriophage coat protein covalently linked to a single-chain T cell receptor mutein.

45. A method of isolating a soluble fusion protein comprising a bacteriophage coat protein covalently linked to a single-chain T cell receptor, the method comprising:

introducing into host cells a DNA vector comprising a sequence encoding the fusion protein,

culturing the host cells in cultured medium under slow induction conditions which permit expression of the fusion protein; and

purifying the fusion protein from the host cell or the medium to isolate the soluble fusion protein.

46. The method of claim 45, wherein the method further comprises contacting an extract of the host cell or the cultured medium with a synthetic matrix capable of specifically binding the fusion protein, and purifying the fusion protein from the synthetic matrix to isolate the soluble fusion protein.

47. A method of isolating a DNA segment comprising a sequence encoding a soluble fusion protein, the soluble fusion protein comprising a bacteriophage coat protein covalently linked to a single-chain T cell receptor, the method comprising:

infecting host cells with a bacteriophage library comprising bacteriophages displaying soluble fusion proteins, wherein each of the fusion proteins comprises the bacteriophage coat protein covalently linked to the single-chain T cell receptor,

culturing the host cells under slow induction conditions which permit propagation of the bacteriophages,

contacting the bacteriophages with a molecule under conditions which permit specific binding between the molecule and at least one of the bacteriophages to produce at least one bacteriophage comprising a specific binding complex,

identifying one of the bacteriophages comprising the specific binding complex,

propagating the bacteriophage; and

isolating the DNA segment from the bacteriophage.

48. The method of claim 47 further comprising inserting the DNA segment into a DNA vector capable of expressing the soluble fusion protein in the host cell.

49. A method of expressing a soluble single-chain T cell receptor, the method comprising:

introducing into host cells a DNA vector comprising a sequence encoding the soluble single-chain T cell receptor,

culturing the host cells in medium under conditions which permit expression of the soluble single-chain T cell receptor; and

purifying the single-chain T cell receptor from the host cell or the medium to isolate the soluble single-chain T cell receptor.

50. The method of claim 49, wherein the host cells are selected from the group consisting of bacterial, insect or mammalian cells.

51. A method of increasing the specific binding affinity of a single-chain T cell receptor for a ligand, the method comprising:

determining a first specific binding affinity between the single-chain T cell receptor and the ligand,

infecting host cells with the bacteriophage library of claim 44, the infecting being under conditions which permit propagation of the bacteriophages,

contacting the host cells with the ligand sufficient to permit specific binding between at least one of the bacteriophages and the ligand to produce at least one specific binding complex between the bacteriophage and the ligand,

identifying one of the bacteriophages comprising the specific binding complex,

isolating DNA from the bacteriophage, the DNA comprising a sequence encoding a soluble fusion protein mutein and expressing the soluble fusion protein mutein,

separating a soluble single-chain T cell receptor mutein from the soluble fusion protein mutein,

determining a second specific binding affinity between the single-chain T cell receptor mutein and the ligand; and

identifying the single-chain T cell receptor with increased specific binding affinity for the ligand as the single-chain T cell receptor mutein in which the second specific binding affinity is greater than the first specific binding affinity.

52. A single-chain T cell receptor, wherein the single-chain T cell receptor is produced by increasing the specific binding affinity of a single-chain T cell receptor for a ligand, the method comprising:

determining a first specific binding affinity between the single-chain T cell receptor and the ligand,

infecting host cells with the bacteriophage library of claim 44, the infecting being under conditions which permit propagation of the bacteriophages,

contacting the host cells with the ligand sufficient to permit specific binding between at least one of the bacteriophages and the ligand to produce at least one specific binding complex between the bacteriophage and the ligand,

identifying one of the bacteriophages comprising the specific binding complex,

isolating DNA from the bacteriophage, the DNA comprising a sequence encoding a soluble fusion protein mutein and expressing the soluble fusion protein mutein,

separating a soluble single-chain T cell receptor mutein from the soluble fusion protein mutein,

determining a second specific binding affinity between the single-chain T cell receptor mutein and the ligand; and

identifying the single-chain T cell receptor with increased specific binding affinity for the ligand as the single-chain T cell receptor mutein in which the second specific binding affinity is greater than the first specific binding affinity.

53. A method of reducing binding between a T cell receptor and a ligand in a mammal, the method comprising:

administering to the mammal a therapeutically effective amount of the single-chain T cell receptor of claim 52.

54. A method of inducing an immune response in a mammal comprising administering to the mammal an effective amount of a single-chain T cell receptor cleaved from a soluble fusion protein comprising a bacteriophage coat protein covalently linked to the single-chain T cell receptor, wherein the immune response is capable of immunizing the mammal against T cell receptor epitopes on the surfaces of pathogenic T cells.

55. A method of preparing an antibody capable of specifically binding a T cell receptor, the method comprising administering to a mammal an effective amount of a single-chain T cell receptor cleaved from a soluble fusion protein comprising a bacteriophage coat protein covalently linked to the single-chain T cell receptor.

56. A method of detecting a molecule capable of specifically binding a T cell receptor, the method comprising:

incubating the molecule with a bacteriophage display library under conditions sufficient to form a specific binding complex between the molecule and at least one bacteriophage in the library, the bacteriophage library comprising bacteriophages displaying fusion proteins, wherein each of the fusion proteins comprises a bacteriophage coat protein covalently linked to a single-chain T cell receptor; and

detecting the specific binding complex as indicative of the molecule capable of specifically binding the T cell receptor.

57. A molecule, wherein the molecule is produced by a method of detecting the molecule capable of specifically binding a T cell receptor, the method comprising:

incubating the molecule with a bacteriophage display library under conditions sufficient to form a specific binding complex between the molecule and at least one bacteriophage in the library, the bacteriophage library comprising bacteriophages displaying fusion proteins, wherein each of the fusion proteins comprises a bacteriophage coat protein covalently linked to a single-chain T cell receptor; and

detecting the specific binding complex as indicative of the molecule capable of specifically binding the T cell receptor.

58. A method of detecting a molecule capable of inhibiting specific binding between a ligand and a T cell receptor, the method comprising:

incubating a soluble fusion protein comprising a bacteriophage coat protein covalently linked to a single-chain T cell receptor, the incubating being in the presence of the ligand,

incubating a soluble fusion protein comprising a bacteriophage coat protein covalently linked to a single-chain T cell receptor, the incubating being in the presence of the ligand and the molecule; and

evaluating the interaction between the ligand and the soluble fusion protein in the absence and presence of the molecule,

wherein less interaction between the fusion protein and the ligand in the presence of the molecule than in the absence of the molecule is indicative of the molecule capable of inhibiting specific binding between the ligand and the T cell receptor.

59. A molecule, wherein the molecule is produced by a method of detecting the molecule capable of inhibiting specific binding between a ligand and a T cell receptor, the method comprising:

incubating a soluble fusion protein comprising a bacteriophage coat protein covalently linked to a single-chain T cell receptor, the incubating being in the presence of the ligand,

incubating a soluble fusion protein comprising a bacteriophage coat protein covalently linked to a single-chain T cell receptor, the incubating being in the presence of the ligand and the molecule; and

evaluating the interaction between the ligand and the soluble fusion protein in the absence and presence of the molecule,
wherein less interaction between the fusion protein and the ligand in the presence of the molecule than in the absence of the molecule is indicative of the molecule capable of inhibiting specific binding between the ligand and the T cell receptor.

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